

REMARKS

Specification Amendments

Applicant submits that a substitute specification was submitted to the USPTO on May 2, 2005. Enclosed is a copy of the postcard receipt received from the USPTO confirming receipt of the substitute specification. However, while a review of PAIR shows entry of the transmittal letter which indicates that a substitute specification was submitted (see “miscellaneous incoming letter” dated May 2, 2005, paragraph 1 (e)), it does not show entry of the actual substitute specification. For the sake of convenience, Applicant has enclosed herewith a duplicate copy of the substitute specification previously submitted on May 2, 2005. Applicant notes that the substitute specification includes SEQ ID NOs in compliance with the requirements of 37 CFR § 1.821 – 1.825. Applicant also notes that the substitute specification was further amended on January 8, 2007.

The substitute specification submitted on May 2, 2005 is further amended in this response to address the objections raised in the present Office Action. Specifically, the specification has been amended to delete the embedded hyperlink on page 3 and to correct several typographical errors in the specification. The typographical errors that were corrected relate to the spacing and labeling of the underlined restriction enzyme sites and primer sequence sites in several of the listed sequences (the names of the restriction and primer sites should be positioned directly under the nucleotides that comprise the site, i.e., the underlined nucleotides). Applicant notes that the term “SEQ ID NO” found adjacent to each of the listed sequences does not include amendment markings (ie underlines) because the “SEQ ID NO” terms were previously added in the substitute specification submitted on May 2, 2005.

No new matter has been added by way of these amendments.

Figure Amendments

Figure 3 was amended to add SEQ ID NOs to the two nucleotide sequences found in the figure (SEQ ID NO: 49 and SEQID NO: 50).

Claim Amendments

Claims 2-26 were previously canceled without prejudice. Claims 39, 40, 46, 47 are canceled herein without prejudice. New claim 54 has been added. Claims 38, 41, and 48-50 have been amended. Claims 1, 27-38, 41-45, and 48-54 are currently pending.

Claim 38 was amended to recite that the library comprises “peptides of 2 to 8 amino acids in length” and that the target protein is “p53”. In addition, claim 38 was amended to recite the additional step of “identifying those cells in which the function of p53 has been restored or modified”. Support for the amendments can be found throughout the specification and particularly at, for example, page 3, lines 9-14 and lines 16-25, pages 5- 8, 10, 12 and Examples 1, 2, 3, and 6.

Claim 41 was amended to recite that the target protein is p53. Support for the amendment can be found throughout the specification, and particularly at, for examples, pages 5- 8, 10, 12 and Examples 1, 2, 3, and 6.

Claims 48-50 were amended merely to correct matters of form. Specifically, claims 48 and 49 were amended to correct their dependencies. Claims 49 and 50 were amended to provide proper antecedent basis.

New claim 54 recites “[a] method of identifying a peptide of 2 to 8 amino acids in length having the ability to restore or modify the function of p53 in an intra-cellular environment comprising: (a) introducing a library comprising nucleic acid constructs encoding peptides of 2 to 8 amino acids in length into host cells having a reporter system that allows for the identification of those cells in which the function of p53 has been restored or modified; (b) identifying a cell in which the function of p53 has been restored or modified; and (c) identifying the peptide in the cell of step (b). New claim 55 recites “[a] method of identifying a peptide of 2 to 8 amino acids in length having the ability to restore or modify the function of p53 in an intra-cellular environment comprising: (a) introducing a library comprising peptides of 2 to 8 amino acids in length into host cells having a reporter system that allows for the identification of those cells in which the function of p53 has been restored or modified; (b) identifying a cell in which the function of p53 has been restored or modified; and (c) identifying the peptide in the cell of step (b). Support for new claims 54 and 55 can be

found throughout the specification and particularly at page 2, line 34 to page 3, line 8, page 7, lines 6-13, and in the Examples of the specification.

The claim amendments are made solely in an effort to advance prosecution and are made without prejudice, without intent to acquiesce in any rejection of record, and without intent to abandon any previously claimed subject matter. No new matter has been added by way of these amendments.

Objection to the Specification

The specification was objected to because it contains an embedded hyperlink. The specification has been amended to delete the embedded hyperlink. Applicant respectfully requests withdrawal of the objection to the specification.

Sequence Rule Compliance

The Office alleged that the specification and drawings recite lists of sequences which sequences are not identified by their corresponding SEQ ID NOs. Applicant submits that a substitute specification was filed on May 2, 2005 which specification includes sequences identified by their corresponding SEQ ID NOs. Applicant submits herewith a duplicate copy of the previously filed substitute application. In addition, Applicant submits herewith a substitute Figure 3 which includes SEQ ID NOs for the two nucleotide sequences found in the Figure. Applicant submits that the instant disclosure is in compliance with the sequence rule requirements of 37 CFR § 1.821 – 1.825. Accordingly, Applicant respectfully requests withdrawal of the further objection to the specification and drawings.

35 USC § 112, Second Paragraph, Rejections

Claims 38-51 were rejected under 35 USC 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter

which Applicant regards as the invention. Specifically, the Office argued that claim 38 omits essential “screening” steps and is therefore incomplete. Without acceding to the merits of the rejection and solely in an effort to advance prosecution, claim 38 has been amended to recite the step of identifying those cells in which the function of the target protein (p53) has been restored or modified, thereby obviating the rejection. Accordingly, Applicant respectfully requests withdrawal of the 35 USC §112, second paragraph, rejection.

35 USC § 102 Rejections

Claims 38-41, 45-47 and 51 were rejected under 35 USC §102(b) as being allegedly anticipated by Shibata et al (EP 0989136). Claims 39, 40, 46, and 47 have been canceled, thus rendering the rejection moot as to these claims. The rejections with respect to claims 38, 41, 45, and 51 are respectfully traversed for the reasons set forth below.

Under 35 U.S.C. § 102(b), a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631, 2 USPQ2d 1051, 10533 (Fed. Cir. 1987); M.P.E.P. § 2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); M.P.E.P. § 2131. Furthermore, the prior art reference must provide an enabling disclosure. M.P.E.P. §2121.01; *In re Hoeksema*, 399 F.2d 269 (CCPA 1968) (“In determining that quantum of prior art disclosure which is necessary to declare an applicant’s invention’ ‘not novel’ or ‘anticipated’ within section 102, the stated test is whether a reference contains an ‘enabling disclosure’ . . .”).

Amended claim 38 and dependent claims 41, 45, and 51 are directed to methods of screening a library of peptides of 2 to 8 amino acids in length for the ability of the library peptides to restore or modify the function of p53. The instant specification explains that “screening a library” implies that it is not known which peptide of the library is introduced into which host cell and the peptides are not introduced in a controlled series. The instant specification further teaches that the library typically has at least 96 different peptide members and preferably has at least 500 different peptide

members. (specification, at page 3, lines 26-37). To anticipate claim 38, the Shibata et al reference must teach a method of screening a library of peptides of 2 to 8 amino acids in length for the ability of members of the library to restore or modify the function of p53 in an intra-cellular environment comprising (1) introducing a library of peptides of 2 to 8 amino acids in length into host cells having a reporter system that allows for the identification of those cells in which the function of p53 has been restored or modified and (2) identifying those cells in which the function of p53 has been restored or modified. As defined in the specification and understood in the art, a “library” of peptides refers to numerous different unknown peptide sequences.

The Shibata et al reference fails to anticipate the present claims because it fails to teach each and every element as set forth in the claims. The Shibata et al. reference is directed to synthesized peptides having a cyclic structure comprising a known sequence found in the C-terminal domain of human p53 protein and having the ability to restore p53 activity. The synthesized peptides are 11 to 17 nucleotides in length. Shibata et al describes methods of individually administering these synthesized peptides to host cells to determine whether they modify the activity of p53. Thus, in contrast to the present invention, the Shibata et al. reference does not teach a method of screening a library of numerous unknown or random peptide sequences of length 2 to 8 nucleotides. Rather, the teaching in Shibata et al. is limited to administering an individual cyclic peptide of known p53 sequence having 11 to 17 nucleotides to a host cell to confirm that the peptide restores p53 activity.

The Office stated that Shibata et al. “teaches introducing ‘test compounds’ (i.e., a library of molecules) into host cells ... which reads on the step of introducing the library into host cells as recited in **clm 38**.” (Office Action at page 5). Applicant respectfully disagrees with this statement. Shibata is in no way “screening a library of peptides”, which by definition refers to a collection of unknown peptides. As taught by the instant specification (and generally known in the art), a method of “screening a library” entails the use of a library that “may have been selected or designed to have certain structural motifs and the nature of individual members of that library can be assumed [however] this phrase implies that it is not known which member is introduced into which cell (or cell sample) and the molecules are not introduced in a controlled series.” (specification

at page 3, lines 26-30). The purpose of screening a library of unknown peptide sequences is to identify those peptides out of a large pool of random peptides that possess the desired function, in this case, those peptides that restore or modify p53 activity. In direct contrast, Shibata describes administering a single synthesized peptide of known sequence to a population of cells to determine whether that peptide restores p53 activity. Unlike in the present invention, the amino acid sequences of Shibata peptides are known before they are administered to cells. Thus, in direct contrast with the definition provided in the instant specification, Shibata teaches a method where it is known which peptide is introduced into which cell and the peptides are introduced in a controlled series. The methods employed by Shibata in no way involve screening a random population of unknown peptide sequences and therefore do not teach a method of “screening a library” as that phrase is defined in the instant specification and otherwise understood in the art.

The Office also stated that Shibata teaches peptides of various amino acids (e.g. Table 1) which read on the peptide of claim 47 having 2 to 8 amino acids because ‘[t]he transitional phrase ‘have’ is interpreted as open-ended and thus the peptides of the instant claims can ‘have’ additional amino acid residues. (Office Action at page 6). While Applicant respectfully disagrees with this interpretation of the claim, it is noted that claim 38 has been amended to recite that the library comprises “peptides of 2 to 8 amino acids in length”. Applicant believes that such language clarifies that the peptide is 2-8 amino acids. The Shibata reference does not read on a peptide of 2-8 amino acids. Virtually all of the Shibata peptides, including the peptides in Table 1, are cyclic peptides of at least 11 amino acids in length. The smaller peptide size offers considerable benefit, particularly in ease of production and ease of delivery.

Given that Shibata et al fails to teach a method of screening a peptide library, much less a library comprising peptides of 2 to 8 nucleotides, it fails to teach each and every element of the claimed method and thus fails to anticipate claim 38 and claims dependent thereon. Accordingly, Applicant respectfully request withdrawal of the 35 USC §102(b) rejections.

35 USC § 103 Rejections

Claims 38-42, 45-47 and 51 were rejected under 35 USC §103(a) as being allegedly obvious over Shibata et al (EP 0989136) in view of Thornborrow et al. (J. Biol. Chem, 274:33747-33756 (1999)). Claims 39, 40, 46, and 47 have been canceled, thus rendering the rejection moot as to these claims. The rejections with respect to claims 38, 41, 42 45, and 51 are respectfully traversed for the reasons set forth below.

Although the Office rejected claims 38-42, 45-47 and 51 as obvious over Shibata in view of Thornborrow, it only specifically addresses claim 42 and refers to its arguments in the 35 102(b) rejection to address the other claims. With respect to claims 38, 41, 45, and 51, Applicant submits that Shibata et al fails to teach or suggest a method of screening a library of peptides of 2 to 8 amino acids in length for the ability of members of the library to restore or modify the function of p53. As discussed above, the teaching in Shibata is limited to a teaching of administering peptides of known sequences to cells which peptides are introduced in a controlled series. Shibata fails to teach or suggest screening a random pool of unknown peptide sequences and therefore fails to teach or suggest teach a method of “screening a library” as that phrase is defined in the instant specification and otherwise understood in the art. Furthermore, the teaching of Shibata is limited to administering cyclic peptides of at least 11 amino acids found in the C-terminal domain of human p53 protein to cells. Thus, Shibata fails to teach or suggest introducing a library of peptides of 2-8 amino acids in length.

The teachings of Thornborrow fail to cure the deficiencies of Shibata. Thornborrow is merely directed to investigations into how p53 transactivates various promoters in different cells types, including the p21 and BAX promoters. Thornborrow does not provide any teachings relating to methods for screening peptide libraries. Thus, there is no teaching in the combined disclosures of Shibata and Thornborrow that would lead one skilled in the art to arrive at a method of screening a library of peptides of 2 to 8 amino acids in length. First, in the absence of any teaching whatsoever that peptides of 2 to 8 nucleotides could be useful in restoring or modifying the function of p53, one skilled in the art would not have been motivated to screen a library of peptides of 2 to 8 amino acids in length. Moreover, nor would one of skill in the art have had a reasonable

expectation of successfully identifying cells in which the function of p53 was restored or modified by screening a library of peptides of 2 to 8 amino acids in length.

With respect to claim 42, the Office stated that Shibata et al teach various methods of screening a library of peptides with a reporter gene assay system as discussed above and stated that Thornborrow et al teach using reporter gene constructs with either a p21 or BAX promoter region that contains p53 response elements. The Office argued that it would have been obvious for one of ordinary skill in the art to use a p21 or BAX promoter region in the reporter gene construct for detecting/measuring/testing p53 activation/function in a reporter gene assay system. However, as discussed above, Thornborrow fails to provide any teachings whatsoever relating to methods of screening peptide libraries. Applicant submits that in the absence of any teaching or suggestion that peptides of 2 to 8 nucleotides could be useful in restoring or modifying the function of p53, one skilled in the art would not have arrived at the method of claim 42 for the reasons discussed above.

Given that Shibata et al and Thornborrow et al., alone or in combination, fail to teach or suggest a method of screening a peptide library, much less a library comprising peptides of 2 to 8 nucleotides, they fail to render obvious claim 38 and claims dependent thereon. Accordingly, Applicant respectfully request withdrawal of the 35 USC §103(a) rejections.

Claims 38-47 and 51 were rejected under 35 USC §103(a) as being allegedly obvious over Shibata et al (EP 0989136) and Thornborrow et al. (J. Biol. Chem, 274:33747-33756 (1999)) in view of Skarnes (US 5,767,336). Claims 39, 40, 46, and 47 have been canceled, thus rendering the rejection moot as to these claims. The rejections with respect to claims 38, 41-45, and 51 are respectfully traversed for the reasons set forth below.

The Office argued that the claims are rendered obvious over Shibata and Thornborrow for the reasons set forth above. However, with respect to claims 43 and 44, the Office stated that the Shibata and Thornborrow references do not explicitly teach the

reporter gene product including a secretion signal peptide or a transmembrane domain as recited in claims 43 and 44. With respect to those claims, the Office stated that Skarnes et al teach reporter gene constructs comprising secretion signals and transmembrane domains. The Office argued that one of skill in the art would have been motivated to generate fusion reporter proteins having secretion signal and transmembrane domains based on the teachings of Skarnes and would have had a reasonable expectation of success in achieving such fusion reporter proteins since all of the cited references demonstrated the success of using the reporter gene assays.

Applicant submits that the teachings of Shibata in combination with Thornborrow do not render the instant claims obvious for the reasons set forth above. The teachings of Skarnes et al. do not cure the deficiencies of Shibata and Thornborrow. Skarnes is directed to vectors and reporter gene products including a secretion signal peptide or a transmembrane domain. Skarnes et al do not mention p53 or the activity thereof and do not provide any teachings relating to methods for screening peptide libraries, much less libraries of peptides of 2 to 8 amino acids in length that restore or modify the function of p53. Thus, there is no teaching or suggestion in the combined disclosures of Shibata, Thornborrow, and Skarnes that would lead one skilled in the art to arrive at a method of screening a library of peptides of 2 to 8 amino acids in length.

Given that Shibata et al, Thornborrow et al., and Skarnes, alone or in combination, fail to teach or suggest a method of screening a peptide library, much less a library comprising peptides of 2 to 8 nucleotides, they fail to render obvious claim 38 and claims dependent thereon. Accordingly, Applicant respectfully requests withdrawal of the 35 USC §103(a) rejections.

Claims 38-51 were rejected under 35 USC §103(a) as being allegedly obvious over Shibata et al (EP 0989136), Thornborrow et al. (J. Biol. Chem, 274:33747-33756 (1999)), Skarnes (US 5,767,336), in view of Noaln (WO 97/27212). Claims 39, 40, 46, and 47 have been canceled, thus rendering the rejection moot as to these claims. The rejections with respect to claims 38, 41-45, and 48-51 are respectfully traversed for the reasons set forth below.

The Office argued that the claims are rendered obvious over Shibata et al, Thornborrow et al, and Skarnes et al for the reasons set forth above. However, with respect to claims 48-50, the Office stated that the Shibata, Thornborrow, and Skarnes references do not explicitly teach introducing a library of nucleic acid constructs into host cells as recited in claim 48, do not teach introducing a library having at least 500 members into host cells as recited in claim 50, and do not teach a library wherein each member has the sequence M-G/M/V-(X)_n as recited in claim 49. With respect to those claims, the Office stated that Noaln et al teach using libraries having the recited features of claims 48-50. The Office argued that one of skill in the art would have been motivated to use libraries having the recited features based on the teachings of Noaln and would have had a reasonable expectation of success in achieving such libraries since all of the cited references demonstrated the success of using reporter gene assays with various elements.

Applicant submits that the teachings of Shibata in combination with Thornborrow, and Skarnes do not render the instant claims obvious for the reasons set forth above. The teachings of Noaln et al. do not cure the deficiencies of Shibata, Thornborrow, and Skarnes. Noaln et al teach the use of nucleic acid libraries generally. Noaln et al. do not mention p53 or the activity or regulation of thereof, and thus do not provide any teachings whatsoever relating to methods for screening libraries of nucleic acid constructs encoding peptides that restore or modify the function of p53, much less peptides of 2 to 8 amino acids in length that modify the function of p53. Thus, there is no teaching or suggestion in the combined disclosures of Shibata, Thornborrow, Skarnes, and Noaln that would lead one skilled in the art to arrive at a method of screening a library of peptides of 2 to 8 amino acids in length that restore or modify the function of p53.

Given that Shibata et al, Thornborrow et al., Skarnes et al., and Noaln et al., alone or in combination, fail to teach or suggest a method of screening a library comprising peptides of 2 to 8 nucleotides that restore or modify the function of p53, they fail to render obvious claim 38 and claims dependent thereon. Accordingly, Applicant respectfully requests withdrawal of the 35 USC §103(a) rejections.

Obviousness-Type Double Patenting Rejections

Claims 38-51 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1 and 28-49 of copending Application Serial No. 10/493,582. Claims 39, 40, 46, and 47 have been canceled, thus rendering the rejection moot as to these claims.

Without acceding to the merits of the rejection, Applicant will consider filing a terminal disclaimer upon notice of an allowable claim. Applicant also reserves the right to address the merits of the rejection upon notice of an allowable claim.

CONCLUSION

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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